REMARKS

Claims 47-52 and 91-99 are pending and stand rejected.

Clarification is requested for the status of claim 50. The Office Action Summary indicates that claim 50 is objected to, but no objections or rejections of this claim are made in the Office Action. Applicants' understanding was that removal of the Section 112 rejection made in the Office Action of November 24, 1999 (Paper No. 14) would result in an indication that claim 50 was allowable.

The amendments are supported by the original disclosure and, thus, no new matter has been added. If the Examiner should disagree, however, she is respectfully requested to point out the challenged limitation with particularity in the next Action so support may be cited in response.

Applicants believe that the phrase "at least one of multiple lineages and other stem cells" in claims 47 and 95 might be confusing because it could be interpreted to read on cells that can generate only a single mature lineage and that cannot generate other stem cells. Support for "which can generate multiple lineages or other stem cells" may be found on page 2, lines 4-7, of the specification.

Because the term "stem cell" is sometimes used in a specific sense that excludes precursor cells and is sometimes used in a generic sense that includes progenitor cells, the recitation of "wherein said stem cells are cells which can generate multiple lineages or other stem cells" in claims 47 and 95 more clearly distinguishes over U.S. Patent No. 5,786,334, which discloses stimulation of progenitor cells but does not disclose stimulation of true stem cells.

Priority Claim

The Office Action advises, "Should Applicant desire to obtain the benefit of the filing date of the prior applications [which resulted in U.S. Patent Nos. 5,939,391 and 6,022,848 which are being newly cited against the subject application], attention is directed to 35 U.S.C. 120 and 37 C.F.R. 1.78" on page 2. Because the subject matter of the pending claims was not disclosed in such applications, claiming their benefit under 35 U.S.C. 120 would confer no benefit. Moreover, it would shorten the term of any patent issuing from the subject application for no purpose. To avoid confusion, it should

be noted that the present application claims benefit under 35 U.S.C. 120 of U.S. Appln. No. 08/627,173, filed April 3, 1996, and this application is a continuation in-part of that parent application.

35 U.S.C. 102 – Novelty

"Anticipation requires identity of the claimed process and a process of the prior art; the claimed process, including each step thereof, must have been described or embodied, either expressly or inherently, in a single reference." *Glaverbel Société Anonyme v. Northlake Marketing & Supply, Inc.*, 45 F.3d 1550, 1554; 33 USPQ2d 1496, 1498 (Fed. Cir. 1995), *citing Scripps Clinic & Research Found. v. Genentech Inc.*, 927 F.2d 1565, 1576, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991). A "new use for either an old compound . . . or an obvious compound" is novel. *See In re Woodruff*, 919 F.2d 1575, 1578, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990), *citing In re Shetty*, 566 F.2d 81, 195 USPQ 753 (CCPA 1977); and *In re Marshall*, 578 F.2d 301, 198 USPQ 344 (CCPA 1978). However "It is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." *In re Woodruff*, 919 F.2d at 1578, 16 USPQ.2d at 1936 (Fed. Cir. 1990), *citing Verdegaal Bros., Inc. v. Union Oil Co. of Calif.*, 814 F.2d 628, 632-33, 2 USPQ2d 1051, 1054 (Fed. Cir. 1987) and *Bird Provision Co. v. Owens Country Sausage, Inc.*, 568 F.2d 369, 375, 197 USPQ 134, 139 (5th Cir. 1978).

Claims 47-49, 51, and 95-96 were rejected under Section 102(b) as allegedly being anticipated by Petrov et al. (U.S. Patent No. 5,786,334). Applicants traverse.

The pending claims are directed to a method of stimulating stem cell proliferation. The specification on page 2, lines 4-7, defines stem cells and distinguishes them from progenitor cells as follows:

> Progenitor cells are able to differentiate into only one or two lineages . . . while stem cells . . . can generate multiple lineages and/or other stem cells.

As seen from the above-quoted passage from Applicants' specification, cells which can generate only a single mature lineage are not stem cells as that term is used in the pending claims. Moreover the pending claims recite that stem cells are cells that can generate multiple lineages or other stem cells.

Petrov discloses stimulating the proliferation of B lymphocytes. B lymphocytes can generate only mature antibody-producing plasma cells and cannot generate other B lymphocytes. Accordingly B lymphocytes are not stem cells. Thus, Petrov does not teach stimulating the proliferation of stem cells.

The Office Action stated on page 3 that "Applicants' arguments concerning progenitor cell definition are not persuasive since the claims do not recite progenitor cells." It is true that the pending claims do not recite progenitor cells because such cells are excluded from the scope of the invention claimed here. But that is exactly the reason why Applicants' arguments should persuade the Examiner that the pending claims are not anticipated. Petrov stimulated the proliferation of B lymphocytes, which are progenitor cells. In contrast, the claimed invention stimulates the proliferation of stem cells that can generate multiple lineages or other stem cells. Thus, the product of proliferation according to the pending claims are not progenitor cells.

The Office Action presents a definition of "stem cell" that is inconsistent with any definition of "stem cells" in Applicants' specification or as recited in the pending claims. Thus, it is an incorrect construction of the pending claims. The Office Action on page 3 defines "stem cells" as follows:

> The term 'stem cells' are interpreted as being cells capable of long term culture as defined in the specification on page 63, lines 17 and 18.

Contrary to the above-quoted passage from the Office Action, many cells capable of long-term culture are neither stem cells nor progenitor cells. The passage cited by in the Office Action actually states, "In the context of BMT [bone marrow transplantation], a hematopoietic stem cell can be defined as one having the ability to generate mature blood cells for extensive periods." There is no reasonable basis for understanding Applicants' specification as interpreting any cell capable of long-term culture as being a stem cell, regardless of its ability to generate mature lineages or other stem cells. In any event, the pending claims recite that stem cells are cells that can generate multiple lineages or other stem cells, and Petrov did not disclose such cells.

The Office Action stated on page 3 that "Applicant's arguments concerning the definition of hematopoietic stem cells is unpersuasive because the cell populations of the instant application would be encompassed by the definition." Respectfully, the only issue is whether Petrov discloses each and every limitation of the claims. The pending

claims recite the use of stem cells that can generate multiple lineages or other stem cells as a result of proliferation. B lymphocytes, the cells disclosed by Petrov for use, cannot generate multiple lineages or other stem cells.

The Office Action's attempt to rely on *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990) is misplaced because the pending claims are directed to a new method, not to the recognition of a previously unrecognized benefit of an old method. Since Petrov does not teach, either expressly or inherently, the stimulation of stem cell proliferation, it does not disclose each and every step of the claimed process. Therefore, the cited reference cannot support a rejection under Section 102.

Claims 47-49, 51-52 and 91-99 were rejected under Section 102(e) as allegedly being anticipated by Tsyrlova et al. (U.S. Patent No. 5,939,391). Claims 47-48, 51-52 and 95-96 have been rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Kozlov et al. (U.S. Patent No. 6,022,848). Applicants traverse both allegations.

The pending claims are directed to a method of stimulating stem cell proliferation comprising contacting hematopoietic cells with a stem cell proliferation stimulating amount of certain compound(s). Tsyrlova and Kozlov have been cited as teaching such compounds "as a stem cell proliferation inhibitor . . . and a method of inhibiting hematopoietic stem cell proliferation . . ." (Office Action, paragraphs 12 and 14). The stimulation of stem cell proliferation is clearly not inherent in the inhibition of stem cell proliferation. Indeed it has not even been asserted that Tsyrlova or Kozlov teach stimulation of stem cell proliferation using any compound. The pending claims are directed to a new method achieving a new result using an allegedly old compound, and as such they are novel under *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

The Office Action's attempt to rely on *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990) is misplaced because the pending claims are directed to a new method achieving a new benefit not actually present in the prior art, not to the recognition of a previously unrecognized benefit of an old method. *In re Woodruff* involved a method for inhibiting the growth of fungi on vegetables by maintaining the vegetables in a certain atmosphere. The prior art cited in *Woodruff* disclosed a method of storing fresh vegetables in order to maintain their fresh appearance by maintaining the vegetables in an atmosphere that overlapped the atmosphere used by Woodruff. In rejecting the argu-

ment that Woodruff's discovery of the fungal-inhibiting benefit of his method conferred patentability, the Federal Circuit stated:

> Judging from the evidence before us, Woodruff may have been the first to recognize the fungal-inhibiting benefit of the method. On the other hand, we do not agree that what Woodruff has allegedly discovered and claimed can be termed a new purpose for performing the claimed method. The generic purpose of the method disclosed in McGill is to prevent the deterioration of fresh vegetables, which certainly encompasses the specific benefit disclosed by Woodruff.

In re Woodruff, 919 F.2d at 1577-78, 16 USPQ2d at 1936 (Fed. Cir. 1990). As seen from the above-quoted passage, the discovery of fungal inhibiting properties did not confer patentability since inhibition of fungal growth was generically encompassed by the inhibition of deterioration taught by the prior art. In contrast, the stimulation of stem cell proliferation in accordance with the pending claims is not encompassed by the inhibition of stem cell proliferation as taught by Tsyrlova and Kozlov.

In fact, *In re Woodruff* supports the novelty of the claimed method, which is directed to a new method of using an allegedly old compound. In holding Woodruff's discovery of a newly recognized advantage of an old method not to be patentable, the Federal Circuit distinguished two earlier decisions on the grounds that they involved a new use for an old or obvious compound, thus affirming that a new use for an old compound is patentable. The Federal Circuit stated as follows:

> The cases of *In re Shetty*, 566 F.2d 81, 195 USPQ 753 (CCPA 1977) and *In re Marshall*, 578 F.2d 301, 198 USPQ 344 (CCPA 1978) do not, as urged by Woodruff, compel a contrary result. In both of these cases, the applicant had discovered a completely new use for either an old compound (Marshall) or an obvious compound (Shetty). In the present case, what Woodruff terms a "new use" (preventing fungal growth) is at least generically encompassed by the prior art purpose of preventing the deterioration of leafy and head vegetables.

In re Woodruff, 919 F.2d at 1578, 16 USPQ2d at 1936 (Fed. Cir. 1990). As seen from the above-quoted passage, the court distinguished between a genuinely new method of use and a use that is generically encompassed by the prior art. The former is novel; the latter is not. The claimed method is a genuinely new use of the type whose novelty was affirmed by the *Woodruff* court because the stimulation of stem cell proliferation is not encompassed by the inhibition of stem cell proliferation taught by the prior art.

Withdrawal of the Section 102 rejections is respectfully requested.

Nonstatutory Double Patenting

Claims 47-49, 51-52 and 91-99 were also rejected under the judicially created doctrine of double patenting over claims 1-3 and 12 of Kozlov et al. (U.S. Patent No. 6,022,848) in view of Tsyrlova et al. (U.S. Patent No. 5,939,391). Applicants traverse for the reasons discussed above with respect to .

Withdrawal of the double patenting rejection is respectfully requested because Applicants' patents neither teach nor suggest the claimed invention as explained above.

The Office Action contains a curious statement that should be addressed on the record. It was stated in the both of the Section 102 and double patenting rejections, "The recitation of the instant application whereby the differentiation of the stem cells is stimulated lends no patentable weight to the claims is a new use for an old method and lends no patentable weight to the claims." (Office Action, numbered paragraphs 12, 14 and 17). Applicants would respectfully suggest that the characterization of the claims as "a new use for an old method" is confusing because it is unclear how a "use" and a "method" are supposed to differ. If the use is new, the method is not old; if the method is old, the use is not new. In any event, the claimed invention is a new method as well as a new use of the composition, as explained above, instead of merely the discovery of a previously unrecognized benefit inherent in the prior art.

Having fully responded to all pending rejections of the Office Action (Paper No. 27), Applicants submit that all claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

Gary R. Tanigawa
Reg. No. 43180

1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

APPENDIX

MARKED-UP VERSION TO SHOW CHANGES

IN THE CLAIMS

The claims are amended as follows.

47. (2 x Amended) A method of stimulating stem cell proliferation comprising contacting hematopoietic cells with a stem cell proliferation stimulating amount of INPROL or an opiate compound or a stem cell proliferation stimulating amount of a combination of INPROL and an opiate compound,

wherein said INPROL is selected from the group consisting of the alpha chain of hemoglobin, the beta chain of hemoglobin, the gamma chain of hemoglobin, the delta chain of hemoglobin, the epsilon chain of hemoglobin, the zeta chain of hemoglobin,

a polypeptide having the sequence of amino acids 1-97 of the human alpha hemoglobin chain,

a polypeptide having the sequence of amino acids 1-94 of the human alpha hemoglobin chain,

Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val, (SEQ ID NO: 1)

Cys-Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Cys (SEQ ID NO: 2) (where the two Cys residues form a disulfide bond),

Asp-Ala-Leu-Thr-asn-Ala-Val-Ala-His-Val-Asp-Asp-Met-Pro-Asn-ala-Leu-Ser-Ala (SEQ ID NO: 3),

Phe-Leu-Gly-Phe-Pro-Thr (SEQ ID NO: 34),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO: 4),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO: 5),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO: 6),

Leu-Val-Val-Tyr-Pro-Trp-Thr (SEQ ID NO: 7),

Leu-Val-Val-Tyr-Pro-Trp (SEQ ID NO: 8),

Leu-Val-Val-Tyr-Pro (SEQ ID NO: 9),

Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO: 10),

Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO: 11),

Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO: 12),

Tyr-Pro-Trp-Thr-Gln (SEQ ID NO: 13), and

Tyr-Pro-Trp-Thr (SEQ ID NO: 28),

wherein said stem cells are cells which can generate [at least one of] multiple lineages or [and] other stem cells.

51. (Amended) A method of stimulating stem cell proliferation comprising contacting hematopoietic cells with a stem cell proliferation stimulating amount of a compound capable of binding opiate receptors, wherein said stem cells are cells which can generate multiple lineages or other stem cells.

95. (Amended) A method of stimulating stem cell proliferation comprising contacting stem cells with a stem cell proliferation stimulating amount of INPROL or an opiate compound or a stem cell proliferation stimulating amount of a combination of INPROL and an opiate compound,

wherein said INPROL is selected from the group consisting of the alpha chain of hemoglobin, the beta chain of hemoglobin, the gamma chain of hemoglobin, the delta chain of hemoglobin, the epsilon chain of hemoglobin, the zeta chain of hemoglobin,

a polypeptide having the sequence of amino acids 1-97 of the human alpha hemoglobin chain,

a polypeptide having the sequence of amino acids 1-94 of the human alpha hemoglobin chain,

Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val, (SEQ ID NO: 1)

Cys-Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Cys (SEQ ID NO: 2) (where the two Cys residues form a disulfide bond),

Asp-Ala-Leu-Thr-asn-Ala-Val-Ala-His-Val-Asp-Asp-Met-Pro-Asn-ala-Leu-Ser-Ala (SEQ ID NO: 3),

Phe-Leu-Gly-Phe-Pro-Thr (SEQ ID NO: 34),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO: 4),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO: 5),

Leu-Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO: 6),

Leu-Val-Val-Tyr-Pro-Trp-Thr (SEQ ID NO: 7),

Leu-Val-Val-Tyr-Pro-Trp (SEQ ID NO: 8),

Leu-Val-Val-Tyr-Pro (SEQ ID NO: 9),

Val-Val-Tyr-Pro-Trp-Thr-Gln (SEQ ID NO: 10),

Tyr-Pro-Trp-Thr-Gln-Arg-Phe (SEQ ID NO: 11),

Tyr-Pro-Trp-Thr-Gln-Arg (SEQ ID NO: 12),

Tyr-Pro-Trp-Thr-Gln (SEQ ID NO: 13), and

Tyr-Pro-Trp-Thr (SEQ ID NO: 28),

wherein said stem cells are cells which can generate [at least one of] multiple lineages or [and] other stem cells.